

PERSISTANT DELIRIUM AS A DISORDER OF SLEEP?

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DISCLOSURE

- HONARIUM FOR PRESENTATION –
BRISTOL MEYERS SQUIBB

DELIRIUM DIAGNOSTIC CRITERIA

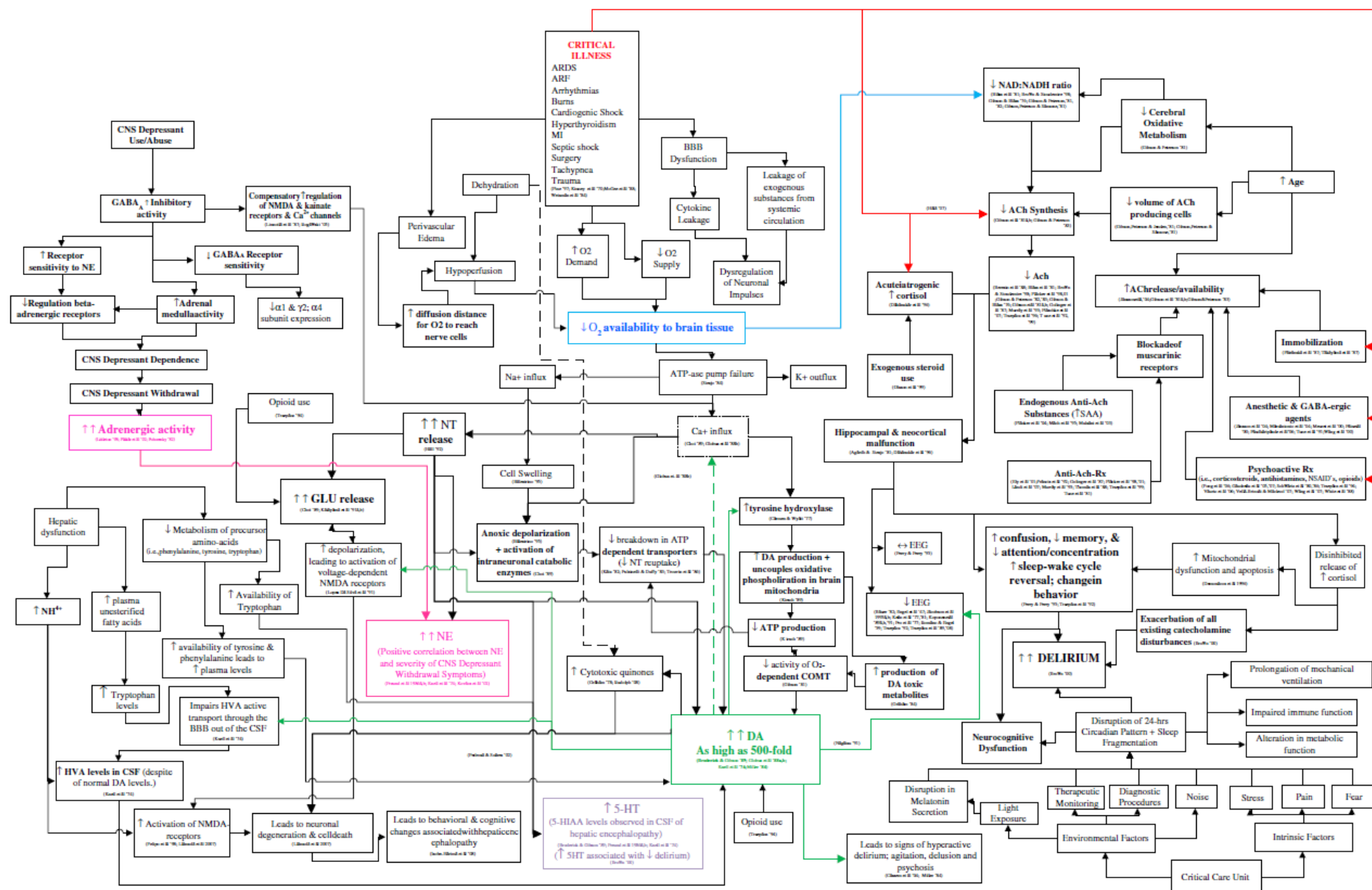
DSM IV

- DISTURBANCE OF CONSCIOUSNESS
- CHANGE IN COGNITION OR PERCEPTUAL DISTURBANCE
- DEVELOPS OVER A SHORT PERIOD OF TIME AND FLUCTUATES OVER THE DAY
- IDENTIFIABLE ETIOLOGY

DSM V

- SIMILAR CRITERIA

INCIDENCE SLEEP DISTURBANCE IN DELIRIUM 92%



NEUROCHEMISTRY/NEUROBIOLOGY OF DELIRIUM

- NEUROCHEMISTRY

ACH	DA	GLU	5HT	MEL	HPA
↓	↑↑	↑	↑↓	↓	↑

- NEUROBIOLOGY

DISRUPTION OF THALAMIC GATING

DISRUPTION OF CIRCADIAN RHYTHMS INCL. SLEEP

Maldonado Advanced Delirium Course 2008

DELIRIUM – MORBIDITY, MORTALITY, PROLONGED HOSPITALIZATION

- MORBIDITY - ↑ INCIDENCE COMPLICATIONS
COGNITIVE IMPAIRMENT
 - 4% Elderly recovered at d/c
 - Cognitive recovery weeks / months
 - Sig. functional decline
 - Residual cognitive impairment = placement
- MORTALITY – 3 fold increase in mortality at one month
- PROLONGED HOSPITALIZATION
 - AVERAGE ↑ length of stay 11 days

PATHOGENESIS OF MORBIDITY / MORTALITY

- PRIMARY PROCESS
- SECONDARY COMPLICATIONS
 - DEHYDRATION
 - STARVATION
 - ASPIRATION PNEUMONIA
 - STASIS ULCERS
 - DVTS / PE
- SELF HARM
- SLEEP DISTURBANCE ?

DELIRIUM / SLEEP DISTURBANCE

- CLINICAL AND PHYSIOLOGICAL RELATIONSHIP

INATTENTION

FLUCTUATING MENTAL STATE

IMPAIRED COGNITION – EXECUTIVE FUNCTION

DELAYED RECOVERY AFTER INSULT IS REMOVED

CRITICAL CARE MEDICINE 2009 13(6) 234

- CHICKEN OR EGG ?

SLEEP DISTURBANCE IN DELIRIUM

- COMMON SYMPTOM IN DELIRIUM
- PREDISPOSING ?
- PRECIPITATING ?
- PERPETUATING ?
- LIMITED STUDIES

Jacobson Jr. of Clin. Sleep Medicine V4(2),2008 137-142

SLEEP DISTURBANCE – CLINICAL LITERATURE

- ANCIENT GREECE - HIPPOCRATES

POSITIVE OUTCOME RELATED TO NORMALIZATION OF SLEEP

- ANCIENT ROME

SIMILAR PERSPECTIVE

TX – TINCTURE OF OPIUM ^{1.}

- CURRENT PERSPECTIVE

MULTIPLE AUTHORS – EMPHASIS ON MANAGEMENT OF SLEEP DISTURBANCE ^{2.}

1.Lipowski Z. Delirium: Acute Confusional States: Oxford University Press 1990

2.Inouye SK Delirium in older persons. N Eng J Med 2006 Mar. 1157-65

STANDARD PHARMACOLOGIC MANAGEMENT-HALOPERIDOL

- ACETYLCHOLINE / DOPAMINE MODEL
Imbalance acetylcholine / dopamine
Tx options - increase acetylcholine
 - physostigmine
 - decrease dopamine activity
 - high potency D2 antagonists
 - ie. Haloperidol dose 1-4 mg

HALOPERIDOL – DRUG OF CHOICE IN DELIRIUM ?

- LEVEL OF EVIDENCE – CATEGORY III
EXPERT OPINION AND ANECDOTE
- PHARMACOLOGIC PROFILE
HIGH POTENCY DOPAMINE BLOCKADE
MINIMAL ALPHA BLOCKADE
MINIMAL ANTICHOLINERGIC EFFECT
MINIMAL SEDATIVE EFFECT

CLINICAL RESEARCH HALOPERIDOL

- PLACEBO CONTROL STUDIES

Haloperidol prophylaxis elderly hip surg.

Decreased duration

Decreased severity

No significant difference in incidence

LOW DOSE HALOPERIDOL OF BENEFIT ¹.

BENEFIT UNLIKELY TO BE SPECIFIC TO HALOPERIDOL
D2 BLOCKADE / NONSPECIFIC EFFECT

1. Kalisvaart KJ Haloperidol prophylaxis for elderly hip-surgery at risk for delirium: a randomized placebo – controlled study J Am Geriatr Soc. 2005 Oct; 53(10):1658-66

CLINICAL RESEARCH HALOPERIDOL VS

- PROSPECTIVE RANDOMIZED STUDIES
OLANZEPINE VS HALOPERIDOL
RESPERIDONE VS HALOPERIDOL
* CHLORPROMAZINE VS HALOPERIDOL
RESULTS = EFFICACY
SMALL N'S

Delirium and Antipsychotics: A systemic review of epidemiology and somatic treatment options. Joseph,D Psychiatry 2008 Oct 5(10)29-36

GENERAL REVIEW ANTIPSYCHOTICS IN DELIRIUM

- RESULTS

ALL ANTIPSYCHOTICS TYPICAL /ATYPICAL(High / Low potency)
APPEAR TO BE EFFECTIVE COMPARED TO BASELINE TX OF
DELIRIUM IN MED / SURG PTS WITHOUT UNDERLYING COG.
DISORDERS

ORAL HALOPERIDOL > FREQUENCY EPS at doses >5 mg/day

Seitz DP, Antipsychotics in the treatment of delirium: a systematic review. J Clin Psychiatry 2007 Jan 68(1):11-21.

NEUROLEPTICS – D2 BLOCKADE VS SEDATION

- HALOPERIDOL - D2 BLOCKADE
- CPZ - SEDATION

(Breitbart - Am. J. Psych 1996 153 (2) 231-237)

Average dose 87 mg

- QUETIAPINE – SEDATION

(Kosliwal – Crit. Care 2010 14(suppl. 1)

Average dose 50 mg

PRIMARY SEDATIVE AGENTS

- **MIANSERIN — COMPARED TO HALOPERIDOL**
PROG. NEURO. PSYCHOPHARMACOL. & BIO. PSYCH. 1995 v20 pp 651-656
- **TRAZADONE FAILED STD. MANAGEMENT**
Jr. of Clin. Psychopharmacology Vol, 18(3) pp 280-282
- **DEXMEDETOMIDINE — COMPARED TO HALOPERIDOL**
Crit. Care 2009 13:R75
- **MELATONIN SURGICAL DELIRIUM**
Prophylaxis and Rx — Statistically +ve vs control
Saudi J. Anaesth. 2010 Sep-Dec 4(3) 160-173

IMPLICATIONS

- D2 blockade – benefit early in clinical course
dose 1-5 mg Haldol equiv.
ongoing benefit ?
- Sedation – (nonbenzodiazepine)
preventive ?
acute/subacute
chronic - residual sleep disorder

SEDATION TIMING

- TREAT MEDICAL CAUSES
- ADD D2 BLOCK IF REFRACTORY
- WAIT DAYS / WEEKS
- ADD SEDATION
- LONGER DURATION – PROLONGED HOSP
MORBIDITY
MORTALITY
- ALTERNATIVE – EARLY INTERVENTION

SEDATIVE OPTIONS

- BENZODIAZEPINES – PPT. / EXACERBATE
- ANTIHISTAMINES – ANTICHOLINERGIC LOAD
- ZOPICLONE – SIMILAR TO BENZOS
- NEUROLEPTICS – QUETIAPINE, CHLORPROMAZINE, NOZINAN, LOXAPINE
- ANTIDEPRESSANTS – TRAZADONE, MIRTAZEPINE
- OTHER - MELATONIN

MANAGEMENT MODEL NEUROLEPTICS

- CL SERVICE VGH
 - NORMALIZE SLEEP
 - CONTROL AGITATION
- WORLD LITERATURE
 - CONTROL AGITATION
 - SLEEP DISTURBANCE – NOT TARGETED
- OUTCOME

GERIATRIC DELIRIUM

WORLD LIT OUTCOME

- MAJORITY INCOMPLETE COG. RECOVERY AT DISCHARGE
- SIG INCIDENCE ALTERNATE CARE
- DURATION HOSP - 11+ DAYS LONGER
- TWO FOLD INCREASE MORTALITY DURING HOSP.

VGH CL PSYCH OUTCOME

- MAJORITY NO CHANGE COG. STATUS AT DISCHARGE
- NO SIG INCIDENCE OF ALTERNATE CARE
- DURATION HOSP - 4 DAYS VS NON-DELIRIOUS
- NO INCREASE MORTALITY

PHARMACOTHERAPY

LOXAPINE MODEL

- DOSES OF LOXAPINE BASED ON

General physical status

BP

Respiratory status

Degree of agitation

Dangerousness

PHARMACOTHERAPY

LOXAPINE MODEL

- REG / PRN DOSE / ROUTES- PO/IM/SC
Old / Old 2.5 q1600 hrs /5.0 mg q2000hrs
PRN 2.5-5.0 mg QIH MAX 30 mg in prns

Old 5.0mg q1600 hrs/ 10 mg q2000 hrs
PRN 5.0-10 mg QIH MAX 75 mg in prns

Young /Old 10 mg q1600 hrs/ 20 mg q2000 hrs
PRN 10-20 mg QIH MAX 160mg in prns

- TITRATION MAX-12.5mg q1600 hrs and 25 mg q2000 hrs

PHARMACOTHERAPY

LOXAPINE MODEL

- SECONDARY SEDATION

Quetiapine 12.5 – 25 mg qhs

25 – 50 mg qhs

Caution higher doses – stim. metab.

TRAZADONE - 25-50 mg qhs

50 – 100 mg qhs

MIRTAZEPINE? - 7.5-15 mg qhs

PHARMACOTHERAPY

LOXAPINE MODEL

- STABILIZATION

Normalization of sleep

Resolution of primary symptoms

Maintain reg dose 24 to 48 hours

- TAPERING-gradual!

$\frac{1}{4}$ total dose q1-2 days

Monitor for re-emergence

VIGNETTES

- SLEEPERS
- SLEEPLESS

SUMMARY

- Sleep disturbance common in delirium
- Predisposing, precipitating, perpetuating?
- Current management D2 block
- Limited research re: sleep in delirium
- No recommendations – pharm. management